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# Intravenous angiography in brain death: report of 140 patients

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**Abstract** We present our experience and discuss the value of cerebral intravenous digital subtraction angiography (IV DSA) in the diagnosis of brain death. A total of 140 patients presenting with clinical signs of brain death were studied by IV DSA. According to the angiographic appearance of the vertebrobasilar system, the patients were divided into four groups. Cessation of blood flow within the internal carotid arteries and their branches was consistently found. Attention is focused on 9 patients with persistent blood flow within the posterior fossa. In sedated patients in whom EEG and evoked brain-stem responses are non-diagnostic, or in order to shorten the observation time, transcranial Doppler should be performed to determine the appropriate moment for IV DSA, which is a reliable method of confirming brain death.

**Key words** Brain death · Cerebral angiography · Intravenous digital subtraction angiography · Circulatory arrest · Brain perfusion

## Introduction

Several conditions must be fulfilled to make the diagnosis of brain death [1]. Clinical determination of death requires irreversible cessation of all function of the entire brain, including the brain stem; thus apnoea (tested for longer than 7 min), dilated pupils, cerebral unresponsivity, absence of cephalic reflexes and EEG silence for 30 min, at least 6 h after an ictus are needed [1, 2]. If any of these criteria cannot be tested or is equivocal, a further test should be performed to confirm the cessation of cerebral perfusion. The absence of blood flow may therefore be used to demonstrate the irreversible state of brain death. Angiography is the definitive technique for assessing cerebral blood flow. We present our experience with cerebral intravenous digital subtraction angiography (IV DSA) in 140 patients. Carotid and vertebral blood flow may be interrupted at the cervical, skull base or intracranial levels. Angiography shows vascular stasis, i.e. no progression of the contrast medium during a prolonged series (of 1 min duration). Several patients, although showing all clinical signs of brain death, nevertheless had a slow posterior fossa circulation.

The increasing use of barbiturate sedation in acute brain trauma explains why EEG and brain-stem tests may not be adequate for the determination of brain death. Various imaging modalities have been used to confirm the diagnosis. Most of these assess cerebral blood flow. Brain swelling and rises in intracranial pressure (ICP) to levels higher than diastolic perfusion pressure [3, 4] lead to circulatory arrest beginning at the cor-

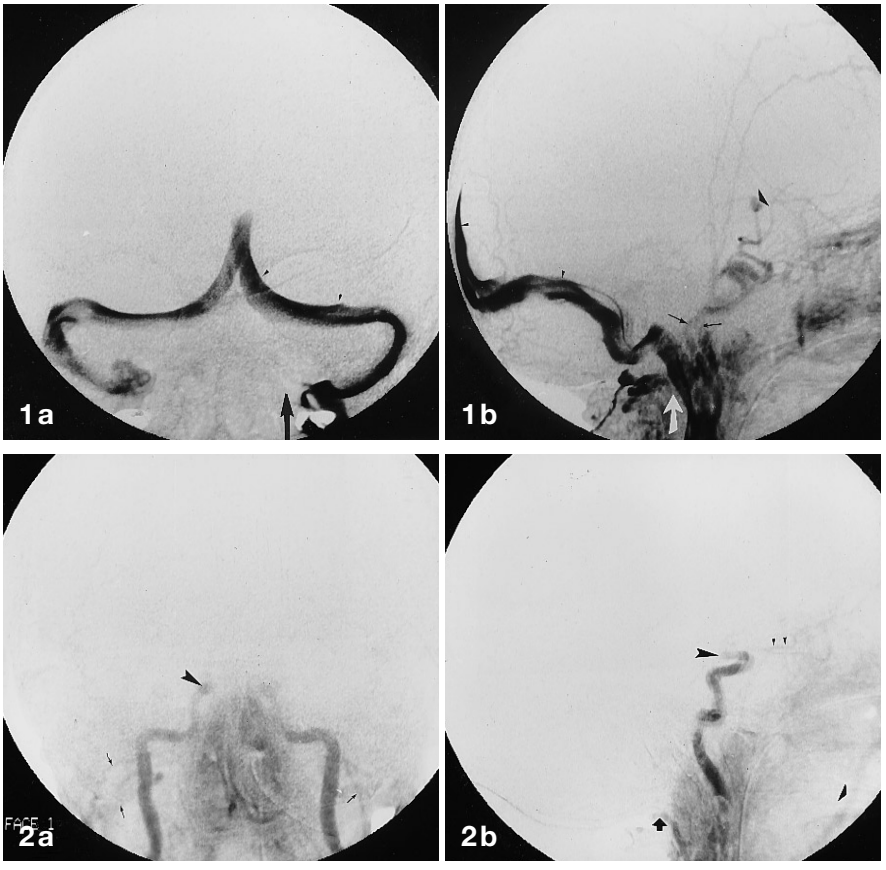


**Fig. 1a, b** A 39-year-old female. Day of admission: acute subarachnoid haemorrhage and intracerebral haematoma. Day 1: absence of brain-stem reflexes; ultrasound: to-and-fro pattern (oscillating flow). IV DSA; contrast medium injected through the left brachial vein. **a** Antero-pasterior view (13th s), **b** lateral view (20th s). This example shows the importance of the injection of the contrast medium into the brachial or the femoral veins and not into the subclavian or jugular veins. **a** shows a minimal left jugular reflux *(black arrow pointing upwards)* into the lateral and sagittal sinuses *(small arrowheads);* **b** shows a partial opacification of both internal carotid arteries *(small arrows)* and a middle cerebral artery aneurysm *(large arrowhead)* in spite of the partial jugular reflux *(white arrow)*

**Fig. 2a, b** A 38-year-old female. Subarachnoid haemorrhage with secondary deep coma. Bilateral unreactive mydriasis meeting the clinical criteria for brain death (including brain-stem function). Electrical silence (EEG) IV DSA **a** AP view (19th s); **b** lateral view (22nd s). Circulatory arrest at C1 level of the carotid siphons *(arrow head)* and at V3–V4 junction of the vertebral arteries (*arrow* in **b**). Normal opacification of the ophthalmic artery (*small arrowheads* in **b**); normal external carotid angiogram (*small arrows* in **a**) with facial vein (*large arrowhead* in **b**)

tical capillary level, and extending progressively to the major branches of the circle of Willis and then to the extracranial arteries [5–8]. When blood flow during diastole is interrupted because of increased ICP, brain oedema results [9]. Raised ICP also impedes venous return and leads to stagnation in the tissues drained by these veins [3]. Blood flow may be imaged using intra-arterial angiography or IV DSA [3–5, 7, 10–17], by means of transcranial Doppler (TCD) [18–22], magnetic resonance imaging (MRI) or angiography (MRA) [23–25], radionuclide cerebral angiography [26, 27] or xenon CT [28, 29]. Brain perfusion is now quantified with SPECT [30, 31] or HMPAO scintigraphic techniques [32].

In unsedated patients presenting with clinical signs of brain death, TCD and electrical silence (EEG) are the most convenient and cheapest modalities for confirming the diagnosis. When these are not available, or in sedated patients, IV DSA or radionuclide angiography may be performed to confirm brain death.

## Patients and methods

Between September 1989 and June 1995, 140 patients, aged 18–68 years, meeting clinical criteria for brain death, were studied by IV DSA from 1 to 12 h after the clinical diagnosis.

Apnoea tests longer than 5 min were performed in 9 cases with slow vertebrobasilar flow. Electrical silence was obtained in only 20 cases. In the remaining 120 cases, EEG recordings could not be obtained mainly because of the use of sedative drugs (60 cases). In all cases, CT revealed the underlying lesions: subarachnoid or intracerebral haemorrhage in 46 (34%), cranial trauma in 69 (49%) and suicide in 14 (10%). A further miscellaneous group of 11 patients (7%) included acute hydrocephalus (3 cases), brain oedema (2 cases), metabolic coma (5 cases), cerebral infarct (1 case) and cardiac arrest (1 case).

When clinical criteria for brain death were met IV DSA was performed in the neuroradiology department next to the intensive care unit.

Contrast medium injections were performed in most cases with a 14 or 16 G needle cannulating a brachial vein (135 cases). In one case, the femoral vein was used. Jugular or subclavian vein injections (4 cases) were associated with massive jugular and dural sinus reflux (Fig. 1) and further injections in a brachial vein were needed. We saw jugular reflux in 6 cases (4.2%): 3 times each with jugular and left brachial injections. From 60 to 80 ml of contrast medium were injected intravenously with an automatic syringe injector at a flow rate of 12–15 ml/s. Simultaneous antero-posterior and lateral or lateral projections alone were performed, each run lasting 60 s; the exposure delay was 6–8 s, or less when the heart rate was

greater than 120 beats/min. The exposure rate was chosen as follows: 1 image/s during the first 15 s, then 1 image/7 s during the remaining 45 s. Assisted ventilation was interrupted during the filming sequences to minimise movements artefacts.

## Results

According to the angiographic appearance of the vertebrobasilar arteries, the patients were divided into four groups. Intravenous angiography was repeated in 5 patients because of persisting blood flow. In 7 patients, both intra-arterial and intravenous angiography were performed; these were at the beginning of our experience.

### Group 1

In 115 patients (Fig. 2), the angiograms showed circulatory arrest at the V3–V4 vertebral level (foramen magnum). The interruption of blood flow occurred at different levels of the internal carotid artery (230 vessels): cervical portion in 100 cases (43%), carotid siphon C5 level (pre-cavernous segment) in 34 cases (15%), carotid siphon C1 level (supra-cavernous segment) in 86 cases (37%) and A1 or M1 segments of anterior or middle cerebral arteries in 10 cases (4%).

When present, opacification of the anterior or middle cerebral arteries was always very slow and restricted to their first (A1, M1) or second (A2, M2) segments. No capillary phase or venous drainage was seen. At the beginning of our experience, intra-arterial angiography was performed in 5 patients, and anterior or middle cerebral artery (A1 or M1 segments) filling was seen.

### Group 2

In 15 patients the contrast medium stasis was seen within the basilar or posterior cerebral arteries, without evidence of flow during the 60-s filming sequence. The basilar and vertebral arteries were compressed against the clivus and the rim of the foramen magnum respectively. Carotid blood flow was interrupted at the C5 level in 1 case, C1 level in 8 cases (Fig. 3) and the A1 or M1 level in 6 cases (Figs. 3, 4).

Normal external carotid venous drainage was present through the superior ophthalmic vein and the cavernous sinus, or via the transverse sinus and the mastoid emissary veins in 15 cases (Fig. 3).

### Group 3

The 9 patients in this group showed delayed and very slow vertebrobasilar blood flow (with venous opacification) and cessation of flow at different internal carotid levels: cervical in 2 cases (Fig. 5), C1 siphon in 1 case and A1 or M1 segments in 6 cases.

This partial but persistent posterior fossa blood flow appears 25–35 s after injection (the normal delay is 3–4 s). In 2 patients, intra-arterial angiography, as well as IV DSA, was performed, with both showing the same features.

The patients met all the clinical criteria for brain death, including cessation of brain-stem function. A 5-min apnoea test was performed in 5 of these cases, EEG in 3 and TCD in 6. IV DSA was repeated in 4 patients 3 h later with identical results.

### Group 4

The remaining case was a false-negative diagnosis of brain death using angiographic criteria in a patient who had undergone craniotomy for acute subdural haematoma. This patient showed all the clinical signs of brain death with electrical silence at EEG. Angiography showed persistent circulation especially on the side of the vault defect.

## Discussion

Arteriography was the first imaging modality used to confirm cerebral circulatory arrest, Heiskanen [3] describing the features in the vertebrobasilar circulation (our group 2). He suggested that a sudden and severe increase in ICP (supratentorial expansion) first affected the cerebrum leading to complete arrest in carotid artery flow. This resulted in tentorial followed by cerebellar herniation, and raised infratentorial pressure with resulting compression of the arteries. The presence of the cerebellar tentorium probably explains this dissociation. When more pronounced, this leads to the features of group 3.

Compared with IV DSA, selective arteriography is more invasive, time-consuming, costly (5 times more than IV DSA) and also requires greater expertise. Vatne et al. [17] showed that increases in intra-arterial pressure associated with arterial injections may push the contrast medium higher in the neck or into the intracranial arteries, giving a false impression of intracranial blood circulation, a finding we also encountered (group 1). TCD of the cerebral circulation [9, 18–22] is very effective but highly operator dependent and the posterior fossa is not fully assessed. It is however a very cheap method (4 times less than IV DSA) which is performed at the bedside and can be be used to determine the exact moment for angiography. Electrophysiological recordings (EEG or evoked brain-stem responses) [33, 34] may be difficult to obtain in an emergency. More-

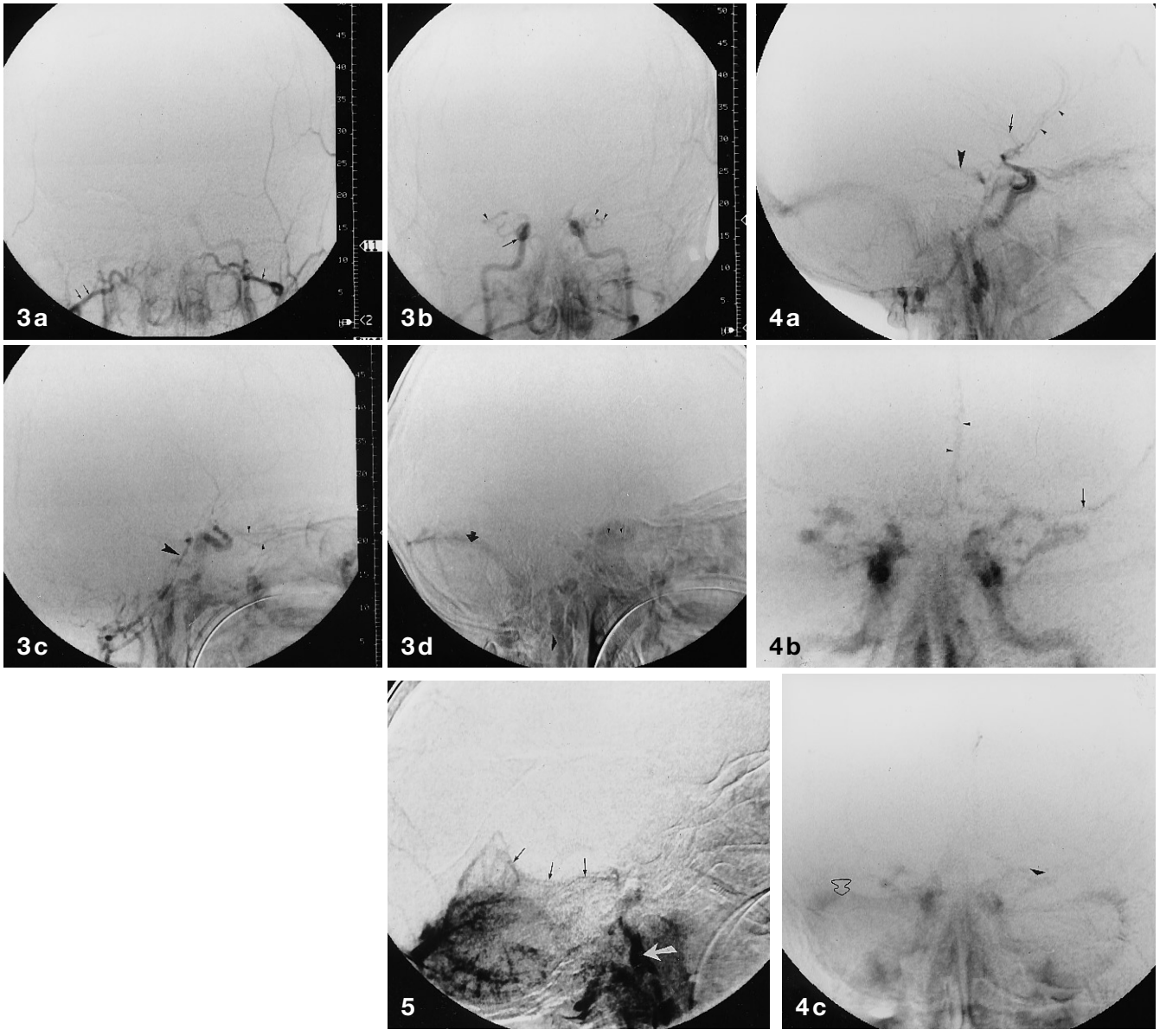


**Fig. 3a–d** A 15-year-old female. Head injury. Day of admission: Glasgow coma scale 6; next day: clinical cessation of cortical and brain-stem functions. IV DSA **a** AP view (12th s), **b** (17th s) **c, d** lateral view (22nd s, 60th s). During angiography, the external carotid branches appear first **a**, then the internal carotid arteries **b, c** with a delay at C1 siphon level *(arrow)* while the basilar artery is stretched and flattened (**c**, *arrowhead*). At 60 s (**d**) note the venous phase of external carotid and vertebral artery angiograms opacifying the lateral sinus *(small arrow)*, the cavernous sinus *(two arrowheads)* and the jugular veins *(large arrowhead)*. Note the absence of supratentorial venous drainage after 1 min

**Fig. 4a–c** A 16-year-old boy. Severe head trauma. Coma with bilateral mydriasis. CT: acute right subdural haematoma with severe brain oedema. Day of admission: clinical signs of brain death. Same day: IV DSA **a** lateral view (17th s); **b, c** AP views (18th s, 26th s). Very delayed opacification of the anterior *(small arrowheads)*, middle *(small arrows)* and posterior cerebral arteries *(arrowhead)*. Normal external carotid venous phase through the ophthalmic veins *(large arrowhead)* and the transverse sinus *(open arrow)* (**c**)

**Fig. 5** A 42-year-old male. Day of admission: severe brain trauma with multiple supratentorial and infratentorial contusions. Day 4: clinical signs of brain death including absence of brain-stem functions. Day 4: IV DSA. Lateral view (17th s). Persistent blood flow with normal cerebellar venous drainage (note the supratentorial downward herniation *(small arrows)* and interruption of flow at the cervical level of the carotid arteries *(white arrow)*

over, barbiturate sedation makes EEG tests non-diagnostic for brain death. Electrical silence lasting 30 min at least 6 h after an ictus is required [1–4].

Since 1975, many authors [26, 27] have reported the value of radionuclide angiography in revealing the absence of cerebral blow flow. As costly as IV DSA, this simple and safe technique, performed at the bedside, has become the imaging method of choice in many countries but is unable to assess the vertebrobasilar system because of its poor resolution. At least 12 h are necessary before repeating a radionuclide study, to allow disappearance of the last dose of 99m-technetium ($^{99m}$Tc) from the circulation [27]. This delay may not be suitable for sequential assessment of cerebral blood flow and may lengthen the observation period. The criteria for brain death are the same as for IV DSA (Fig. 2).

Since 1983, many reports [11–17] of the value of IV DSA in confirming brain death have appeared. However, the techniques described have varied, mostly in the duration of the filming sequence: 12 s [13], 20 s, [12, 17], 30 s [16], 45 s [3] 1 min [10] or not mentioned at all [14]. The length of these filming sequences must be compared with those of the $^{99m}$Tc scintigraphy technique (30 s) [26, 27], xenon CT (4–5 min) [28, 29], MRI (3 min) [23–25] and HMPAO SPECT (30–40 min) [30]. The longer the filming sequence, the more accurately can the irreversibility of the process be determined. Absence of jugular or sinus reflux is an important factor in the reproducibility of IV DSA. This jugular reflux appears much more frequently when jugular injection is performed (75 %), than with brachial injection (2.5 %), and is about the same as that found with radionuclide cerebral imaging using $^{99m}$Tc (1.2–3.5 %) [35]. No reflux was seen by Van Bunnen et al. [12] in their series (110 cases). In the other series which had fewer patients (3–13 cases), the contrast medium was delivered directly into the inferior vena cava [13, 17] or into the right atrium in neonates [15, 16, 34]. Massive jugular reflux with pooling of contrast medium within the dural venous sinuses should not be considered as a reliable sign of cerebral death [35]. The injection site must be modified and the study performed again.

Like the other techniques using an intravenous injection, $^{99m}$Tc [26, 27, 32], xenon CT [28, 29], and SPECT [30, 31], IV DSA is a physiological, and also reproducible imaging method [12]. In our experience, a confirmatory diagnosis could always be made in optimal conditions and further injections because of jugular reflux were rarely needed. However, contrast is poor in cases with severe tachycardia (greater than 120 beats/min), and adjustments must be made using shorter delay times and higher injection flow rates to compensate for the decreasing cardiac ejection volume.

Angiography, arterial or IV DSA, however, has several drawbacks [26, 29]: patients must be moved to the radiology department whereas radionuclide imaging methods can be performed in the intensive care unit [27]. The amount of contrast medium, even if moderate (60–80 ml) may also theoretically precipitate renal failure especially with underlying cardiovascular instability.

Grouping our patients as described above according to the level of the circulatory arrest was useful for greater understanding and clarification. These groups were very similar to those presented by Alvarez et al. [11] and by others using xenon CT [28, 29]. Complete absence of hemispheric and posterior fossa circulation was noted in group 1. These patients lost their cortical and brain-stem functions (group 1 of Aschwal et al.) [28]. In group 2, there was contrast medium stasis within the vertebrobasilar and carotid systems. The complete absence of capillary and venous filling was the constant feature [7, 8]. In their group 3, there was persistent and delayed posterior fossa blood flow; this pattern is similar to the patients in our group 3 [28]. Ashwal et al. [28] were more radical in their study of cortical perfusion with xenon CT: in cases of absence of cerebral blood flow but with partially preserved brain-stem flow, hemispheric circulatory arrest was diagnosed in spite of persisting brain-stem reflexes (including respiratory). In our 9 patients, the diagnosis of brain death was only made when patients met all the clinical criteria including the apnoea test of 5 min [1]. Our experience and repeated angiograms have shown that major circulatory delay precedes a circulatory arrest. This dissociation (carotid arrest but continued posterior fossa circulation) may illustrate the protecting effect of the cerebellar tentorium when increasing hemispheric pressure leads to bilateral carotid circulatory arrest [3, 4, 6, 7, 9]. Even without the angiographic criteria for the posterior fossa, clinical signs (apnoea tests included) and other laboratory studies helped us to diagnose brain death (electrical silence in 3 cases [33–34], to-and-fro pattern on Doppler ultrasound in 6 [9, 18–22]). Our false-negative case was related to the craniotomy. In 1963, Heiskanen [3] showed that the normal filling was due to the effects of the skull defect without raised ICP. Alvarez et al. [11] postulated that raised ICP was severe enough to induce brain death, and that true perfusion after craniotomy did not occur at the microvascular level even after cerebral perfusion pressure restoration. Our data support his view.

In conclusion, imaging can be used for establishing the cause of coma, and may be desirable when objective documentation is needed to substantiate clinical findings, or to shorten the period of observation required before organ donation. IV DSA appears to be a reliable and simple imaging aid in the diagnosis of brain death. It should never be interpreted alone, without considering the clinical signs and the various exploratory tests of brain-stem function.

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